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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/608,304	06/27/2003	Michel J. N. Cormier	80892(303655)	8982
77069	7590	05/01/2008		
Edwards Angell Palmer & Dodge LLP (Zasano Pharma Inc. - 303655) P.O. Box 55874 Boston, MA 02205			EXAMINER	
			ALSTRUM ACEVEDO, JAMES HENRY	
			ART UNIT	PAPER NUMBER
			1616	
			MAIL DATE	DELIVERY MODE
			05/01/2008 PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/608,304

Applicant(s)

CORMIER ET AL.

ExaminerJAMES H. ALSTRUM
ACEVEDO**Art Unit**

1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 January 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) _____ is/are pending in the application.
- 4a) ☐ Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 6/27/03 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 2/28/08
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1-2 and 8-28 are pending. Applicants amended claims 1, 9, 11-12, 15, 17-18, 20-21 and 24. Applicants previously cancelled claims 3-7. Receipt and consideration of Applicants' new IDS (submitted 2/28/08), amended claim set, and remarks/arguments submitted on January 23, 2008 are acknowledged. All rejections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments. Applicants' claim amendments have necessitated new grounds of rejection (e.g. under §103(a)).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2 and 8-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trimmer et al. (WO 96/10630) in view of Godshall et al. (U.S. Patent No. 5,879,326), Darouiche (U.S. Patent No. 6,162,487) and Patel et al. (U.S. Patent No. 6,248,363).

Applicant Claims

Applicant claims a method of coating the hydrophobic surface (e.g. metallic) of one or more microprojections or a microprojection array comprising (1) providing a microprojection array having hydrophobic surfaces; (2) treating the surface by rinsing with a solution containing an amphiphilic wetting agent including a hydrophilic group and a hydrophobic group; (3) providing a coating formulation; (4) applying said coating formulation to one or more microprojection surfaces; and (5) drying said coating formulation onto said surface.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Trimmer teaches a method of introducing a biological material (i.e. active material) into a predetermined target cell population comprising providing (a) a plurality of inert microprobes (i.e. microprojections) positioned on a support (i.e. an array), (b) a solid or quasi-solid mass of

target cells defining an interface with the microprobes, and (c) a biological material at the interface, and the physically contacting the cells with the microprobes to cause the microprobes to non-lethally pierce the cell walls and/or membranes of the cells. The target cells may be contacted by the microprobes *in vitro* or *in situ*. This method is applicable to virtually all cell types and any biological material capable of being introduced into cells described therein (abstract). **The biological materials can be applied to the microprobes and/or support or substrate in several ways, including the direct deposition of a film or coating** with standard techniques (pg. 11, lines 24-31). Trimmer speculates that any liquid material, which wets the substrate surface, will be trapped as a meniscus between the microprobes and this effect can be enhanced by adding wetting agents to the solution of biological material, or to the medium in which the method is carrier out (pg. 11, line 35 through pg. 12, line 3). In Example 1, Trimmer teaches the fabrication of the microprobes from silicon wafers including the following steps: (1) **cleaning** with a mixture of HCl and **hydrogen peroxide (i.e. a wetting agent)**; (2) oxidation by **heating** in an electrically heated quartz furnace; (3) **etching in buffered hydrofluoric acid**; (4) cascade rinsing; and (5) **etching in an aqueous solution of KOH (i.e. an alkaline solution)**.

Godshall teaches that microprotrusion devices, in addition to being fabricated from silicon substrates, may also be fabricated from plastics/polymers **and metals** utilizing well known micromachining, microfabrication, and MEMS technologies (col. 5, lines 57-65).

Darouiche teaches the coating of medical devices with a combination of antiseptics and antiseptic coating (title, abstract). Darouiche teaches that conventional coating techniques typically involve application or absorption of a layer of surfactant, such as **tridodecylmethyl ammonium chloride** (TDMAC) surfactant, followed by coating with an antimicrobial layer.

Suitable methods of applying the surfactant include soaking the device in a solution of TDMAC air drying, and rinsing with water, prior to application of the drug coating (col. 2, lines 11-32). This procedure broadly reads on Applicants step of rinsing a device surface with a solution of wetting agent. Surfactants are wetting agents.

Patel teaches that it is known that both lipophilic and hydrophilic surfactants are known to be useful **for improving both the physical and chemical stability of active ingredients** as well as enhancing absorption and bioavailability (col. 10, lines 42-64). Patel provides a variety of lipophilic and hydrophilic surfactants as well as the corresponding HLB values, if known: polyethoxylated fatty acids (Table 1, col. 12-col. 14), PEG-fatty acid diesters (Table 2, col. 13, line 40 through col. 15, line 12), PEG-fatty acid mono- and di-ester mixtures (Tables 3 and 4, col. 15, line 12 through col. 16, line 44), alcohol-oil transesterification products (Table 5, col. 16, line 45 through col. 18, line 67), polyglycerized fatty acids (Table 6, col. 19), propylene glycol fatty acid esters (Table 7, col. 19), mixtures of propylene glycol esters-glycerol esters (Table 8, col. 21, lines 1-20), mono- and di-glycerides (Table 9, col. 22, line 1 through col. 23, line ~10), sterol and sterol derivatives (Table 10, col. 23, line ~10), PEG-sorbitan fatty acid esters (Table 11, col. 24, lines 30-67), PEG-alkyl ethers (Table 12, col. 25, line 1-25), sugar esters (Table 13, col. 25, line 25-43), PEG alkyl phenols (Table 14, col. 25, lines 43-60), **polvoxyvethylene-polvoxypropylene block copolymers (i.e. poloxamers)** (Table 15, col. 25, line 60 through col. 27, line 33), sorbitan fatty acid ester surfactants (Table 16, col. 27, lines 35-54), and lower alcohol fatty acid esters (Table 17, col. 27, line 55 through col. 28, line 10).

Trimmer lacks the teaching of rinsing a hydrophobic (e.g. metallic) surface with a solution of wetting agent prior to coating (this applies only to claims 1-2 and 8-23). This deficiency is cured by the combined teachings of Godshall, Darouiche, and Patel.

***Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)***

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to modify the teachings of Trimmer to utilize a metal substrate in the fabrication of microprotrusions, because metals were known in the art as being suitable for the fabrication of microprotrusion devices (Godshall). An ordinary skilled artisan would have had a reasonable expectation of successfully using metal to make microprotrusion devices, because metallic materials were taught by the prior art as being suitable in the fabrication of microprotrusion devices. Regarding the step of rinsing with an amphiphilic wetting agent, the prior art recognized that prior to coating of metallic surfaces of medical devices it was desirable to adsorb surfactant (i.e. wetting agent, such as TDMAC) by rinsing said medical device in a solution of said surfactant (Darouiche). Patel demonstrates that a wide array of surfactant (i.e. amphiphilic materials) was known at the time of Applicants' invention. The use of any of these known surfactants (e.g. poloxamers) would have been prima facie obvious, because rinsing of medical device surfaces (e.g. hydrophobic metallic surfaces) with surfactants was taught by the prior art. As a consequence of this teaching an ordinary skilled artisan would have had a reasonable expectation of success when applying a solution of any known surfactant, because all surfactants are amphiphilic molecules and by definition have surface active properties (i.e. surfactant = surface active agent) and thus would reasonably be expected to interact with both

hydrophilic and hydrophobic surfaces. The critical micelle concentration (CMC) of many surfactants and the methods needed to ascertain said concentrations are known in the art. It would have been well within the skill of the artisan to determine the CMC and use said concentration of a known surfactant within a formulation (See, for Example, Dominguez et al. "Determination of Critical Micelle Concentration of Some Surfactants by Three Techniques," *J. Chem. Educ.* **1997**, 74(10), 1227 (Abstract). Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Response to Arguments

Applicant's arguments with respect to claims 1-2 and 8-23 have been considered but are moot in view of the new ground(s) of rejection, set forth above.

Claims 24-28 **remain rejected** under 35 U.S.C. 103(a) as being unpatentable over Trimmer et al. (WO 96/10630) in view of Haji et al. (US 2001/0018272) for the reasons of record, which have been restated below.

Applicant Claims

Applicants claim a method of coating a surface or one or more microprojections of a microprojection array comprising (i) providing a microprojection array, (ii) treating the surface with a method selected from the group consisting of chemical pre-etching, plasma treatment,

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heat treating, and rinsing with an alkaline detergent (iii) providing a coating formulation, and (iv) applying said coating formulation to said treated surface, and (v) drying the coating formulation onto said surfaces to form a coating.

Determination of the Scope and Content of the Prior Art
(MPEP §2141.01)

The teachings of Trimmer were restated above in the instant office action.

Haji teaches a plasma treatment apparatus/method and that **plasma treatment is known for etching the surface of semi-conductor wafer and cleaning a surface of a printed circuit board** (title; abstract; [0002]). An exemplary mixture for plasma etching gases includes a mixture of SF₆ and He gases [0051].

Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)

Trimmer lacks the teaching of plasma treating a surface prior to coating. This deficiency is cured by the teachings of Haji.

Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)

It would have been *prima facie* obvious to a person of ordinary skill at the time of the instant invention that plasma treating a silicon substrate, such as the substrate used by Trimmer to make microprobes, prior to coating would essentially clean the surface of any undesirable

organic compounds and remove any native oxide present on the silicon surface. An ordinary skilled artisan would have been motivated to modify the teachings of Trimmer to utilize plasma treatment as an alternative or even supplemental pre-conditioning treatment prior to application of a coating formulation, because this is an art recognized conventional step. It would have been apparent to the ordinary skilled artisan that exposure of the fabricated microprojections to any of the methods taught by Trimmer or plasma treatment taught by Haji, albeit for shorter periods of time than those required in fabrication, would remove extraneous impurities and yield a "clean" surface ideally suited for coating. A skilled artisan would have had a reasonable expectation of successfully forming a film of the biological materials taught by Trimmer on his invented microprobes, because plasma treatment is well known as being able to etch silicon surfaces, and the step of drying a coating formulation is conventional in the formation of coatings. Applicants' data in the specification was noted. Applicants have not claimed any unexpected or surprising results.

Response to Arguments

Applicant's arguments filed January 23, 2008 have been fully considered but they are not persuasive. Applicants traversal of this rejection is based on their assertions that (1) there is "no authority" (understood as implying "reason") to expect that plasma treatment applied to silicon surfaces would "clean" the surfaces and (2) none of the cited references teach the same motivation or expected end result of plasma treatment.

The Examiner respectfully disagrees with Applicants' traversal arguments. Regarding (1), the only authority required is recognition by the ordinary skilled artisan that etching (i.e. removal of the surface native oxide layer) would also remove anything found on said native

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oxide layer (i.e. it would clean the surface). Regarding (2), the prior art is not required to teach the same motivation. Application of the same technique to the microprotrusion surface is reasonably expected to yield the same results. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., hydrophobic surfaces) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Conclusion

Claims 1-2 and 8-28 are rejected. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J.H.A.-A.

Patent Examiner

Technology Center 1600

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616